REMARKS

Initially, Applicants wish to thank the Examiner for the careful consideration given this case. Claims 1-20 are currently pending in this case and are addressed herein. Applicants gratefully acknowledge the withdrawal of the species election requirement. By amendment herein, Claims 1, 7, 11, and 17 have been amended. By amendment herein, Claim 2 is cancelled without prejudice to later presentation in this or related cases. It is hereby asserted that no new matter has been introduced through any amended claims. Applicant gratefully acknowledges the allowability of Claims 8-10, 15, and 16.

This response addresses those issues raised in Office Action of November 6, 2002. In light of the amendments and comments presented herein, it is believed that all pending claims are allowable, and timely notice to such effect is respectfully requested.

Objections

The Examiner objects to Claim 7 because the convention of putting a space between the amino acid residues was not consistently employed. Applicants' Agent thanks the Examiner for noticing this typographical error. Claim 7 has been amended to reflect the Examiner's suggestion. Reconsideration and withdrawal of the objection is respectfully requested. Given that Claim 7 was not rejected in view of any prior art, it is submitted that Claim 7 is presently allowable and notice to that effect is respectfully requested.

35 U.S.C. §112 rejections

The Examiner rejects Claims 11-14 and 17-20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner notes that Claim 11 recites the limitation "therapeutic agent" which lacks antecedent basis in Claim 7. The Examiner further notes that Claim 17 recites the limitation "fragment" which lacks antecedent basis in Claim 7. Claims 11

and 17 have been amended to sufficiently address these issues. Reconsideration and withdrawal of the rejection of Claims 11-14 and 17-20 is respectfully requested.

35 U.S.C. §§ 102 and 103 rejections

Claim 1 has been amended to include the limitation of dependent Claim 2, namely that the peptide fragment is not greater than fifty amino acid residues in length. The Remarks on Examiner's rejections under 35 U.S.C. §§ 102 and 103 should be considered in light of this amendment.

On multiple occasions as detailed below, the Examiner rejects the present claims on the assumption that a peptide that contains amino acids having the charge motif of positive-positive-neutral hydrophobic would bind selectively to tumor-derived endothelial cells. As the Examiner is surely aware, the three dimensional folding of peptides may obscure a particular motif from the external portion of the peptide. Indeed, as stated in paragraph 32 of the present specification, "interaction between the peptide and its target molecule may be weakened due to many degrees of conformational freedom as well as the peptide being 'hidden' by the fusion protein." The same principle applies to the peptides cited by the Examiner. Accordingly, simply because a motif is contained within a peptide, there is no guarantee that the motif is configured properly within the larger peptide to allow the motif to bind selectively to tumor-derived endothelial cells. In addition, even if a peptide that contained such a motif were to bind to tumor-derived endothelial cells, there is no indication that it would do so selectively, as is specified in the present claims.

The Examiner appears to assume that it is an inherent property of the cited peptides to bind selectively to tumor-derived endothelial cells. As is stated in § 2112 of the MPEP, "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (citations omitted; emphasis in the original.) Section 2112 of the MPEP goes on to quote *In re Robertson*, 169 F.3d

743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' 'Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " (citations omitted) The same section of the MPEP further quotes *Ex part Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990), "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." (emphasis in the original)

It is respectfully submitted that the Examiner has not provided reasonable support that the property of binding to tumor endothelial cells - let alone specific binding to tumor endothelial cells – is an inherent property presented by the applied prior art. It is further submitted that it is very unlikely that the peptides of the applied prior art possess that property, given the well known number of targets throughout the numerous cells of the body to which the peptides could bind. The number of peptides which were identified and described in accordance that have specific binding to tumor-derived endothelial cells with the embodiments of the present invention further supports this point. The FliTrx™ library which was used in the disclosed studies to identify the various embodiments of the present invention contains 1.77×10^8 primarily clones (*see* attached documentation). Out of these only 38 were found to bind specifically to tumor-derived endothelial cells (*see* Fig. 4 of the present specification).

The Examiner rejects Claim 1 under 35 U.S.C. § 102(b) as being anticipated by Xu et al. The peptide described in Wu et al. is 183 amino acids in length. Accordingly, the peptide disclosed by Xu et al. does not contain each and every limitation of the amended Claim 1, thus, obviating any possible 102 rejection. Reconsideration and withdrawal of this rejection is thus respectfully requested.

The Examiner rejects Claims 1 and 2 under 35 U.S.C. § 102(a) as being anticipated by Oh, Yoo et al., or Lee et al. Claim 2 has now been cancelled without prejudice. As the Examiner notes, the information provided by the Accession Number documentation does not indicate that the peptide would selectively bind to tumor-derived endothelial cells. As outlined above, there is no reason to assume that this is an inherent property of the peptides disclosed in the three references. Accordingly, the three references do not contain each and every limitation of the amended Claim 1 and a 102 rejection is thus obviated. Reconsideration and withdrawal of this rejection is respectfully requested.

The Examiner rejects Claims 1, 3, 4, and 6 under 35 U.S.C. § 102(e) as being anticipated by Godowski et al. or Goddard et al. The peptides that are employed by Godowski et al. are antibodies, which are larger than 50 amino acids in length (*See e.g.*, Figs. 3A and 3B in Godowski et al.). The peptides that are described by Goddard et al. also contain greater than 50 amino acids in length (*See e.g.*, Figs. 3A and 3B in Goddard et al.). Accordingly, neither reference contains each and every element of the currently amended Claim 1 and, by extension, of the dependent Claims 3, 4, and 6. Reconsideration and withdrawal of this rejection is thus respectfully requested.

The Examiner rejects Claims 1 and 3-6 under 35 U.S.C. § 103(a) as being unpatentable over Godowski et al. in view of Thorpe et al., or Goddard et al. in view of Thorpe et al. As stated above, the limitation of Claim 2 has been incorporated into Claim 1. Accordingly, the present rejection is completely obviated since Claim 2, and its subject matter, were not addressed in the rejection, and since Claims 3-6 properly depend from Claim 1. Reconsideration and withdrawal of this rejection is thus respectfully requested.

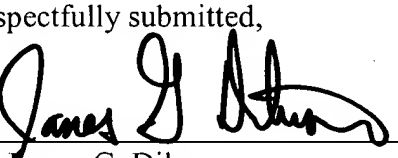
By the enclosed amendments and remarks, Applicant has fully addressed all of the issues raised by the Examiner in the Office Action mailed on November 6, 2002. In view of the amendments and remarks included herein, it is respectfully submitted that the present

application is in condition for final allowance and notice to such effect is respectfully requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below.

The references made of record, but not applied in rejecting any claims of the instant application, have been reviewed. Applicants acknowledge that the Examiner has deemed such references not sufficiently relevant to have been relied upon in the outstanding Office Action. However, to the extent that the Examiner may apply such references against the claims in the future, Applicants are prepared to fully respond thereto.

Respectfully submitted,

Dated: February 6, 2003

By 

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AMENDMENTS (MARKED-UP VERSION)

IN THE CLAIMS:

Please cancel Claim 2 without prejudice to this or related cases.

Please rewrite Claims 1, 7, 11, and 17 as follows:

1. (amended) A purified peptide fragment with selective binding to tumor-derived endothelial cells, wherein the peptide fragment possesses a charge motif of positive- positive- neutral hydrophobic (++O), wherein the peptide fragment is not greater than fifty amino acid residues in length.

7. (amended) A composition useful for targeting tumor-derived endothelial cells, said composition comprising a peptide selected from the group consisting essentially of SEQ ID NO 1 Cys-Gly-Gly-Arg-His-Ser-Gly-Gly-Cys; SEQ ID NO 2 Cys-Gly-Gly-Arg-Lys-Leu-Gly-Gly-Cys; SEQ ID NO 3 Cys-Gly-Gly-Arg-Arg-Leu-Gly-Gly-Cys; SEQ ID NO 4 Cys-Gly-Gly-Arg-Arg-Ser-Arg-Gly-Gly-Cys; and SEQ ID NO 5 Cys-Leu-Leu-Arg-Arg-Ser-Arg-Leu-Leu-Cys.

11. (amended) The composition of Claim 8[7], wherein the therapeutic agent includes at least one agent selected from the group consisting essentially of anticellular agents, chemotherapeutic agents, radioisotopes, and cytotoxins.

17. (amended) The composition [purified peptide fragment] of Claim 7, wherein the said peptide [purified peptide fragment] is linked to a diagnostic agent that is detectable upon imaging.